STATEMENT OF WORK

PART I – BACKGROUND

In some past Regulatory Impact Analyses (RIA) of air pollution regulations, EPA has estimated the mortality impact of reductions in tropospheric ozone levels for inclusion in a primary estimate of the overall benefits of the regulations. In more recent analysis, EPA has relegated the ozone mortality effect estimate to a sensitivity analysis, due to concerns about double-counting with an estimate of mortality related to reductions in ambient $PM_{2.5}$ levels. While the growing body of epidemiological studies suggests that there may be a positive relationship between ozone and premature mortality, there is still substantial uncertainty about this relationship. The evidence linking premature mortality and particulate matter is currently stronger than the evidence linking premature mortality and ozone, because of this, it is important that models of the relationship between ozone and mortality include a measure of fine particulate matter as well. Because of the lack of monitoring data on fine particles or their components the measure of particulate matter used in most studies was generally either PM_{10} or TSP or, in some cases, Black Smoke. If a component of PM, such as $PM_{2.5}$ or sulfates, is more highly correlated with ozone than with PM or TSP, and if this component is also related to premature mortality, then the apparent ozone effects on mortality could be at least partially spurious.

In the recent RIA, the ozone mortality sensitivity estimate was calculated using results from four U.S. studies (Ito and Thurston, 1996; Kinney et al., 1995; Moolgavkar et al., 1995; and Samet et al., 1997), based on the assumption that demographic and environmental conditions on average would be more similar between these studies and the conditions prevailing when the nonroad standards are implemented. The studies were combined using probabilistic sampling methods to estimate the impact of ozone on mortality incidence. Weights used in the probabalistic analysis were derived using a random-effects model (DerSimonian and Laird, 1986).

A recent analysis by Thurston and Ito (2001) reviewed previously published time series studies of the effect of daily ozone levels on daily mortality and found that previous EPA estimates of the short-term mortality benefits of the ozone NAAQS (U.S. EPA, 1997) may have been underestimated by up to a factor of two. The authors hypothesized that much of the variability in published estimates of the ozone/mortality effect could be explained by how well each model controlled for the influence of weather. Weather is a potentially important confounder of the ozone/mortality effect, and Thurston and Ito found that earlier studies using less sophisticated approaches to controlling for weather consistently under-predicted the ozone/mortality effect. They found that models incorporating a non-linear temperature specification appropriate for the "U-shaped" nature of the temperature/mortality relationship (i.e., increased deaths at both very low and very high temperatures) produced ozone/mortality effect estimates that were both more strongly positive (a two percent increase in relative risk over the pooled estimate for all studies evaluated) and consistently statistically significant. Further accounting for the interaction effects between temperature and relative humidity produced even more strongly positive results. Inclusion of a PM index to control for PM/mortality effects had

little effect on these results, suggesting an ozone/mortality relationship independent of that for PM. However, most of the studies examined by Ito and Thurston only controlled for PM_{10} or broader measures of particles and did not directly control for $PM_{2.5}$. As such, there may still be potential for confounding of $PM_{2.5}$ and ozone mortality effects, as ozone and $PM_{2.5}$ are highly correlated during summer months in some areas. In the SAB September, 2001, advisory on the draft analytical blueprint for the second Section 812 prospective analysis, the SAB cited the Thurston and Ito study as a significant advance in understanding the effects of ozone on daily mortality and recommended re-evaluation of the ozone mortality endpoint for inclusion in the next prospective study (EPA-SAB-COUNCIL-ADV-01-004, 2001).

The EPA methodology can be updated by using a more comprehensive set of ozone mortality studies that includes studies with controls for nonlinear temperature effects, as well as appropriate controls for fine particle exposure, as well as applying a more appropriate statistical method for pooling the VSL estimates. For example, the empirical Bayes meta-analysis model implemented by Levy, Hammitt, and Spengler (2000) enables the overall mean and distribution of the ozone mortality effect to reflect the underlying variability of the individual effect estimates. The purpose of this purchase order is to provide an updated assessment of the ozone mortality literature and estimates of the mean and distribution of the ozone mortality effect estimates.

PART II – TASKS

Task 1:   Estimation of Pooled Ozone Mortality Effect Estimate

The consultant shall review the available literature on the relationship between ozone and mortality, to be provided by the EPA WAM. The consultant shall use empirical Bayes meta-analysis techniques to combine reported coefficient estimates from the epidemiological literature, taking into account potential confounding by co-pollutants, especially $PM_{2.5}$, temperature, and other time-varying variables that may be correlated with ambient ozone levels. The reanalysis must consider the most recent literature which has included controls for ambient $PM_{2.5}$ exposure, but may also consider other literature using single-pollutant specifications or controls for PM_{10}. The result of the analysis should be a distribution or distributions of ozone C-R function coefficients that can be used to robustly estimate the mortality impact of a reduction in ambient ozone concentrations.

Task 2:   Meta-regression

Pooled effect estimates can provide an improved central tendency estimate of the ozone mortality effect, but do not systematically address between-study variability that may be associated with choice of estimation method and model, study location, target population, and demographic and risk characteristics. Meta regression analysis has been widely applied in the health literature to pool results from clinical studies to examine how key factors influence health

outcomes. The contractor shall use the empirical Bayes meta-regression approach, as described in Levy, Hammitt, and Spengler (2000), to provides further adjustment to the posterior estimates developed in Task 1, by specifying the estimates as a function of study characteristics plus a between study variability term. The result of this analysis should be a set of conditional distributions describing the relationship between the ozone mortality effect and underlying study characteristics, including temperature specification, co-pollutants, and study demographics, e.g. age or health status of the population.

PART III – DELIVERABLES

Task 1:

The contractor shall produce a report and a database detailing the results of (1) the empirical Bayes estimation of adjusted ozone mortality effect estimates, and (2) the resulting composite distribution of the ozone mortality effect estimates. The contractor shall deliver to the project officer draft results suitable for submission to a peer-reviewed scientific journal and the supporting database within 2 months of award.   Based on comments from the Project Officer and any peer-reviewers, the contractor shall resubmit draft manuscript and the supporting database no later than December 31, 2003.

Task 2:

The contractor shall produce a report and a database detailing the results of the second stage empirical Bayes meta-regression exploring the relationship between variability in ozone mortality effect estimates and study-specific factors. The contractor shall deliver to the project officer a draft report suitable for submission to a peer-reviewed scientific journal and the supporting database within 3 months of award.   Based on comments from the Project Officer and any peer-reviewers, the contractor shall resubmit draft manuscript and the supporting database no later than January 30, 2004.